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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/762,629	01/22/2004	Sherin S. Abdel-Meguid	P50897D1	5050

7590 12/21/2006

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EXAMINER	
JIANG, DONG	
ART UNIT	PAPER NUMBER
1646	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/21/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/762,629	ABDEL-MEGUID ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19 and 27-32* is/are pending in the application.

4a) Of the above claim(s) *31 and 32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19 and 27-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *19 and 27-32* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/22/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Applicant's species election without traverse of SEQ ID NO:12 and 4. Accordingly, claims 31 and 32, as non-elected inventions, are withdrawn from consideration. Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141.

Currently, claims 19 and 27-32 are pending, and claims 19 and 27-30 are under consideration. Claims 19 and 27-30 will be examined to the extent that they read on the elected sequence.

Formal Matters:

Information Disclosure Statement

Applicant's IDS submitted on 1/22/04 is acknowledged and has been considered. A signed copy is attached hereto.

Priority acknowledgement

This application claims benefit of U.S. application 09/914,695 filed on 8/31/01, and U.S. provisional application 60/125,299 filed on 3/19/99, which is acknowledged.

Specification

Title

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the elected claims are directed.

Priority application

The specification is objected to because the status of U.S. Application 09/914,695, which has been issued as U.S. Patent No. 6,706,487, has not been updated yet.

Rejections under 35 U.S.C. 112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19 and 27-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 19 is indefinite for the recitation "an effective amount" because it is unclear for what effect specifically the amount is effective, and how the "effective amount" can be determined, as there is no specific disease or condition recited, which would be treated with the said antibody (only "autoimmune disease", which encompass many distinct diseases/disorders). The metes and bounds of the claim, therefore, cannot be determined. The claim is further indefinite for the recitation "in need thereof" because it is unclear of what is needed. The claim is further indefinite for the recitation "an *altered antibody*" because it is unclear what it is meant. A "definition" of such is noted in the specification, which states that it "refers to a protein encoded by an altered immunoglobin coding region", and "such altered antibodies are engineered antibodies (*e.g.*, chimeric or humanized antibodies) or antibody fragments ..." (page 6, the first paragraph). However, such fall within the intended definition (exemplary), and are not considered, in themselves, to provide definitive meanings for the term. The claim is further indefinite for the recitation "the framework regions ... are derived from *at least one selected antibody* ..." because it is unclear what it is meant, for example, it is unclear how antibody is selected, and how many antibodies may be involved. The claim is further indefinite for the recitation "*less than about* 3.9 x 10^{-11} M" because it is unclear as to what molar range is covered by the term "about", for example, is 4 or 5 x 10^{-11} M "less than about 3.9 x 10^{-11} M"? The metes and bounds of the claim, therefore, cannot be determined.

The remaining claims are included in this rejection because it is dependent from the specifically mentioned claims without resolving the indefiniteness issue belonging thereto.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19 and 27-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited in scope to a method of treating autoimmune diseases associated with IL-18 with an altered antibody comprising the heavy chain of SEQ ID NO:10 and the light chain of SEQ ID NO:2, or comprising the CDRs of the antibody 2C10 (as indicated in Figures 1 and 2), or with the specific antibody disclosed by the prior art, does not reasonably provide enablement for claims to a method of treating any or all autoimmune diseases with any or all altered antibodies to IL-18. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Claim 19 is directed to a method of treating conditions associated with autoimmune diseases using an altered antibody to IL-18 with a dissociation constant equal to or less than about 3.9×10^{-11} M, which reads on a method of treating conditions associated with any or all autoimmune diseases using an altered antibody to IL-18 with a dissociation constant equal to or less than about 3.9×10^{-11} M. However, not all conditions associated with autoimmune diseases are related to excess IL-18. Therefore, antagonizing IL-18 may not be suitable for treating any or all autoimmune diseases. Further, with respect to the altered antibody with a dissociation constant equal to or less than about 3.9×10^{-11} M, the specification merely discloses one antibody, 2C10, meeting the limitation of the claim, and no other altered antibodies meeting the limitation of the claim was ever identified or particularly described in the specification. It is well established in the art that it is impossible to predict the structure of the antibodies with a particular dissociation constant (as encompassed by the claimed genus in the present claims), or to predict the dissociation constant of an antibody, which is also well demonstrated in the instant

specification. For example, the specification discloses three "altered" antibodies, and they are, besides 2C10, 14B7 and 13G9. Neither 14B7 nor 13G9 meets the limitation of having "a dissociation constant equal to or less than about 3.9×10^{-11} M". Further, the specification does not provide a repeatable method for obtaining the claimed antibody, nor instruction or guidance as to how to make the antibodies commensurate in scope with the claim, and thus, one skilled in the art would not know how to make the encompassed antibodies in its full scope based on the instant disclosure, and would not be able to practice the claimed method in a manner commensurate in scope with the claim. It would require undue experimentation.

Due to the large quantity of experimentation necessary to determine which autoimmune diseases are suitable for anti-IL-18 antibody treatment, and to identify additional said antibodies as recited in the claims, and possibly screen same for said dissociation constant; the lack of direction/guidance presented in the specification regarding same; the absence of working examples directed to same; the state of the prior art indicating that it is impossible to predict the structure of the antibodies with a particular dissociation constant, or to predict the dissociation constant of an antibody; the unpredictable and complex nature of the invention, and the breadth of the claims which embraces all autoimmune diseases, and a potentially broad class of antibodies with unknown structure, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 19, 27, 29 and 30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 19 is directed to a method of treating conditions associated with autoimmune diseases using an altered antibody to IL-18 with a dissociation constant equal to or less than about 3.9×10^{-11} M, wherein the "altered antibody" reads on any or all altered antibodies with said dissociation constant. Claims 29 and 30 merely require the antibody having a partial CDR from the CDRs of 2C10 antibody (for example, 5 amino acids, SEQ ID NO:12). However, the specification merely discloses one antibody, 2C10, meeting such a limitation of the claim, and no

other altered antibodies meeting the limitation of the claim was ever identified or particularly described in the specification.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In the instant case, the only factor present in the claims is a "functional" characteristic, i.e., a dissociation constant (for binding affinity), and the structure of the antibodies with said particular dissociation constant is not defined (claim 19), or partially defined (claims 29 and 30). As neither the structure of the antibodies with a particular dissociation constant nor the dissociation constant of an antibody can be predicted, the skilled artisan cannot envision the sequence structure of the encompassed antibody genus, with the exception of the antibody 2C10. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the encompassed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

In the instant application, only the antibody comprising the CDRs of the antibody 2C10 (as indicated in Figures 1 and 2), but not the full breadth of the claim (an altered antibody to IL-

18 with a dissociation constant equal to or less than about 3.9×10^{-11} M) meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 19 and 27 are rejected under 35 U.S.C. 102(e) as being anticipated by Nishida et al., US 2002/0128450 A1.

Nishida discloses an artificially produced antibody peptide capable of neutralizing the biological activities of IL-18, wherein the peptide comprises a part or the whole of the variable regions in anti-IL-18 antibody, including, among others, humanized antibodies (the abstract). Further, Nishida teaches that the anti-IL-18 antibody used for generating the altered antibody peptide, #125-2HmAb, is made from mice (Example 1, pages 7-8). Furthermore, Nishida teaches that the artificially produced antibody peptide is capable of inhibiting IFN-γ induction by IL-18 at IC50 less than 100 pM (Figure 5), and useful as pharmaceutical to treat diseases such as multiple sclerosis and rheumatoid arthritis (abstract, and page 6, the left column). As such, the reference anticipates the claims. Note, although Nishida does not specifically mention the binding affinity of the antibody peptide, Nishida's antibody peptide has the similar neutralizing activity as that of the present 2C10 antibody as shown in Table I (page 25) of the specification, the IC50 of 2C10 is 0.1 nM (100 pM). As such, Nishida's antibody peptide would inherently have a dissociation constant equal to or less than about 3.9×10^{-11} M in the absence of evidence to the contrary.

Conclusion:

No claim is allowed.

Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Dong Jiang, Ph.D.
Patent Examiner
AU1646
12/18/06